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| APPLICATION NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTY. DOCKET NO. |
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| 09/103,745 | 06/24/98 | AGRAWAL | [illegible] |

EXAMINER

HM12/0909

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BOSTON MA 02109

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | 4 |

DATE MAILED: 09/09/99

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

## OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) 1-4 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-4 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: 1

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☒ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

**--SEE OFFICE ACTION ON THE FOLLOWING PAGES--**

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 5,856,462. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons: each the instant application and patent '462 teach the same oligos except that the instant application refers to such oligos as part of a composition in claims 1 and 2. Such compositions would have been obvious in view of the oligo since the oligos to be delivery to cells would necessarily be in the form of a composition such as the oligo in a buffer or water. Thus the oligo and the compositions there of are obvious one over the other.

The instantly claimed invention is also drawn to a method of inhibiting gene expression via the oligos of each the instant application and the parent patent cited above. The oligos of the '462 patent, being the same oligos of the instant claims, in a method of inhibiting gene expression would have been an obvious use for the oligos at issue since this was what they were developed and intended for, and such functionality also be attributed to the oligos in the claims of parent patent '462.

Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Each of the claims recite the language "composition of matter". Such language is considered indefinite since it is not readily apparent what limitation the language embraces, thus the mete and bounds of the claimed composition can not be determined. Referring to the composition of the claims as a "composition of matter" seems redundant since all compositions/compounds are necessarily "matter" per se. Referring to the compositions simply as "compositions" would be remedial.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reduced side effects for the CpG oligos having the modifications listed in claim 2 and/or shown in Example 2, does not reasonably provide enablement for CpG oligos having simply phosphorothioate linkages as in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Note Example 2 in the specification where applicants teach that the modifications as shown in claim 2 provide for reduced side effects in rats only and when compared to CpG oligos having phosphorothioate linkages. No other data is presented that CpG oligos having simply phosphorothioate linkages as in claim 1 provide for reduced side effects in vivo. In fact example 2 of the specification as filed appears to show that such oligos as in claim 1 provide from worse

side effects. Thus such oligos do not appear to be enabled for the functionality claimed.

Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods in cells in culture and for reduced side effects for the CpG oligos having the modifications listed in claim 2 and/or shown in Example 2, does not reasonably provide enablement for methods in whole organisms and for CpG oligos having simply phosphorothioate linkages as in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claimed invention is drawn to methods of inhibiting gene expression via the claimed oligos in any context in vitro and in vivo (whole organism) such that reduced side effects are obtain in view of the oligos administered, and further a method which claims the same but additionally contemplates further treatment effects to be obtained. The specification as filed teaches the delivery of oligos to rats, but to no specific target gene sequence for inhibition. No inhibition of gene expression of any kind is shown. However, Example 2 demonstrates reduced side effects for the oligo modifications of claim 2 and Example 2 compared to oligos having just phosphorothioate linkages in rats.

The ability to determine regions of accessibility and delivery regimes in vivo for antisense oligos such that any desired target gene can be successfully inhibited and/or treatment effects be provided remains to date a highly unpredictable endeavor in the art. Such factors as determination of nucleic acid secondary and subsequent structure for accessible regions to antisense in vivo and

delivery such that a target gene in particular tissues, cells, etc. can not be accurately predicted, and further such that treatment effects may be provided against any disorder (see Branch and Crooke). De novo trial and error experimentation would have to be engaged in order top practice the invention as claimed drawn to in vivo gene inhibition and treatment against any disorder since the unpredictable factors cited for in vivo antisense applications have no general guidelines for their engineering. Effectively each new antisense and/or gene to be inhibited require empirical trial and error determination of accessible regions in vivo as well as how to deliver the oligo to a whole organism such that target tissues and cells may receive sufficient quantities of oligos such that the gene of interest may be inhibited and/or treatment effects be provided. The specification as filed does not provide such general guidelines so as to resolve the known unpredictable factors for antisense.

The claimed invention is further not enabled in view of the issues regard claim 1, which claims 3 and 4 are dependent on, as set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Krieg et al. (WO 96/02555 or Antisense or Nucleic Acid Drug. Devel.).

Claims 1 and 2 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Zhao et al.

Each Krieg et al. (WO 96/02555 or Antisense or Nucleic Acid Drug. Devel.) or Zhao teach CpG oligos as claimed.

Claim 1 is rejected under 35 U.S.C. 102(b) as being clearly anticipated by Krieg et al (Nature).

Krieg teach CpG phosphorothioate oligos.

The prior art of record and searched does not teach specific inhibition of gene expression or treatment effects related to antisense gene inhibition utilizing CpG oligos as the antisense.

Note that applicant intend to rely upon previous application 08/711,568, now U.S. Patent 5,856,462; however, it is not clear in what capacity. If applicants intend to name continuing or CIP status of said parent in the instant application, applicants are required to amend the first line of the specification to indicate the relation to said parent and to update the status of the application as the issued patent. CIP status requires naming the application in the oath under section 120 along with a "duty to disclose" clause as per section 120. Correction is required. Note that such continuing data should include the relation of the PCT application named in the transmittal papers filed on 6/24/98.

Any inquiry concerning this communication should be directed to John L. LeGuyader at telephone number (703) 308-0447. Please note that the examiner's compressed workweek day off is every Friday.

John L. LeGUYADER
September 8, 1999

JOHN L. LeGUYADER
PRIMARY EXAMINER
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